UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/931,836	08/16/2001	Luc Desnoyers	P3030R1C1	5218

9157 7590 03/12/2003

GENENTECH, INC.
1 DNA WAY
SOUTH SAN FRANCISCO, CA 94080

EXAMINER	
JIANG, DONG	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/12/2003

10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/931,836	DESNOYERS ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED OFFICE ACTION

Applicant's preliminary amendment filed on 01 February 2002 is acknowledged and entered. Following the amendment, the original claims 1-21 are canceled, and the new claims 22-34 are added.

Currently, claims 22-34 are pending and under consideration.

Formal Matters:

Priority

This application claims priority to US provisional application 60/115,552, and PCT/US00/05601 (see paper No. 9). For the following reasons, the Examiner finds that the present claims 22-41 are not supported in the manner required by 35 U.S.C. 101 and 112, first paragraph by all of the prior applications, thus the present claims are not entitled to the benefit of the filling date of all of the prior applications.

The priority application 60/115,552, filed on 12 January 1999, merely discloses the nucleic acid sequence of SEQ ID NO:1 encoding PRO1484 polypeptide, and the amino acid sequence of PRO1484 (SEQ ID NO:2), and indicates that the polypeptide has homology to adipocyte complement-related protein. The prior application 60/115,552 fails to provide any specific, substantial and credible utility for the claimed PRO1484 polypeptide, and provides no guidance or working examples to teach how to used the claimed invention. Therefore, the Examiner is not able to establish that the priority document 60/115,552 satisfies the utility/enablement requirement of 35 U.S.C. 101/112, first paragraph. As such, the claims of the instant application are not entitled to the benefit of the filling date of prior application 60/115,552. Priority is granted to the filing date of the later application, PCT/US00/05601, filed on 01 March 2000, wherein some specific and substantial biological properties of said PRO1484 polypeptide were disclosed, such as inducing re-differentiation of chondrocytes (Example 36).

Title

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are directed.

Claims

Applicant's attention is directed to 37 CFR 1.821. (d), which reads as follows:

> Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing " in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

Claims 22-31 are objected to under 37 CFR 1.821. (d) for identifying a nucleotide sequence by a figure with SEQ ID NO: in parenthesis. The correct format to define a sequence structure is by referring to its SEQ ID NO. Correction is required.

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22-27, 30 and 31 recite "the extracellular domain". However, the protein identified as PRO1484 is a soluble protein, and is not disclosed as being expressed on a cell surface. Accordingly, the limitation that the claimed protein comprises the "extracellular domain" is indefinite, as the art does not recognize soluble proteins as having such domains. Further, if the protein had an extracellular domain, the recitation of "the extracellular domain ..., lacking its associated signal sequence" (claim 22, part (d), for example) is indefinite as a signal

sequence is not generally considered to be part of an extracellular domain, as signal sequences are cleaved from said domains in the process of secretion from the cell.

The remaining claims are rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22-27, 30, 31, 33 and 34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited in scope to a polypeptide of SEQ ID NO:2, and a polypeptide of SEQ ID NO:2 lacking its associated signal peptide, does not reasonably provide enablement for claims to various % variants SEQ ID NO:2 (claims 22-26, for example), and a fragment of the extracellular domain of SEQ ID NO:2 (claims 22-27, 30 and 31, for example), which do not have a functional activity, or do not have the same functional activity as SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are directed to % variants, or a fragment of the extracellular domain thereof, which read on any or all variants meeting the sequence limitation, and encoding polypeptides either with or without a functional activity. The claims encompass an unreasonable number of nucleic acids encoding inoperative polypeptides. However, while the specification teaches that PRO1484 polypeptide of SEQ ID NO:2 is capable of inducing re-differentiation of chondrocytes (Example 36), it provides no guidance or working examples as to how the skilled artisan could use a nucleic acid encoding an inactive polypeptide variant or fragment of SEQ ID NO:2, as no functional limitation associated with the variants in the

claims. The working example, Example 37, is noted, which indicates that PRO1484 polypeptide of SEQ ID NO:2 is capable of *affecting* glucose or FFA uptake by skeletal muscle cells. However, such example cannot be used to support enablement issue of the invention as "affecting" does not clearly specify the functional property PRO1484 possesses, and the specification teaches that it could be either stimulating or inhibiting glucose or FFA uptake. As such, one of skilled in the art would not know how to use the claimed invention based upon that example.

With respect to the fragment of "the extracellular domain", the specification indicates PRO1484 is a secreted protein, and does not define such domain, therefore, it is unclear whether such domain exists, and what kind of functional property it may possess. The specification provides no guidance or working example as to how to make and use such a fragment.

Due to the large quantity of experimentation necessary to determine how to use the nucleic acids encoding inoperative polypeptides, and the small fragments thereof, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which embrace a broad class of structurally diverse variants and fragments, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 22-27, 30, 33 and 34 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 22-27, 30, 33 and 34 encompass variant polypeptides having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence, such as SEQ ID NO:2, or "an extracellular domain" of SEQ ID NO:2 (claims 22-27, parts (c) and (d), for example). The claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity. The specification

merely discloses *one* amino acid sequence of human PRO1484 with SEQ ID NO:2. No variants, "an extracellular domain" or other PRO1484 fragments thereof meeting the limitation of the claim were ever identified or particularly described.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In the instant application, applicants have a single polypeptide with a specific function that have not been correlated to any particular structural regions. Therefore, only isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO:2, but not the full breadth of the claims (variants and fragments) meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Rejections Over Prior Art:

The following rejections under 35 U.S.C. §§ 102 and 103 are made in view of the determination that the effective filing date for the instantly claimed invention is 01 March 2000, which is the filing date of the application of PCT/US00/05601.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 22-27, 30 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Dumas et al., WO 99/06551-A2.

Dumas discloses a human secreted protein having an amino acid sequence of SEQ ID NO:307, which comprises amino acids 1-124 of SEQ ID NO:2 of the instant invention with 100% sequence identity (see computer printout of the search results). The cited sequence, therefore, anticipates claims 22-27, 30 and 31 as being a polypeptide having a sequence identity to the amino acid sequence of the extracellular domain of the polypeptide of SEQ ID NO:2.

Claims 22-24, 30 and 31 are rejected under 35 U.S.C. 102(a) as being anticipated by Strachan et al., WO 99/55865-A1.

Strachan discloses a rat skin cell protein having an amino acid sequence of SEQ ID NO:280, which comprises amino acids 1-105 of SEQ ID NO:2 of the present invention with 93.3% sequence similarity (see computer printout of the search results). The cited sequence, therefore, anticipates claims 22-27, 30 and 31 as being a polypeptide having at least 90% sequence identity to the amino acid sequence of the extracellular domain of the polypeptide of SEQ ID NO:2.

Claims 22-24, 30 and 31 are rejected under 35 U.S.C. 102(e) as being anticipated by Strachan, US 6,150,502, for the same reason above as the pertained disclosure in the patent is identical to that in WO 99/55865-A1.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 33 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dumas et al., WO 99/06551-A2; Strachan et al., WO 99/55865-A1; or Strachan, US 6,150,502 as applied to claims 22-27, 30 and 31 above, and further in view of Capon et al. (US 5,116,964).

The teachings of the primary references are summarized above. None of the primary references specifically teaches a recombinant fusion protein comprising an immunoglobulin Fc region, and the target protein.

Capon discloses a novel polypeptide comprising an immunoglobulin Fc region, and a target protein sequence (column 5, lines 13-20). The cited reference indicates that fusion of a target protein to a stable plasma protein such as an immunoglobulin constant domain extends the in vivo plasma half-life, and facilitate purification of the protein (column 4, lines 38-43, and column 5, lines 13-20).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to make "a fusion protein comprising the target protein and an immunoglobulin Fc region as taught by Capon. One of ordinary skill in the art would have been motivated to make the Fc fusion protein because it would improve the therapeutic value of the protein (with prolonged in vivo plasma half-life), and facilitate purification of the protein as suggested by Capon, and reasonably would have expected success in view of Capon's disclosure, in which various genes had already been expressed successfully in their systems at the time the invention was made.

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
Patent Examiner
AU1646
3/3/03